



Food and Drug Administration  
CBER/OCBQ/DMPQ/LAC  
HFM-673  
1401 Rockville Pike  
Rockville, MD 20852

**Date:** June 25, 1999

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**Subject:** Chemical Test Results for Michigan Department of Public Health, Anthrax Vaccine Adsorbed, Lots FAV020 and FAV030

**To:** Neil Goldman, Ph.D. HFM-20

Aluminum was measured by flame atomic absorption spectrophotometry on June 17, 1999. CBER's results are as follows:

<u>Lot #</u>	<u>mg Al/mL</u>
FAV020	1.30
FAV030	1.33

The limit for aluminum as stated in Title 21, Sec. 610.15 of the Code of Federal Regulations is no more than 0.85 mg of aluminum in the recommended individual dose when determined by assay or no more than 1.14 mg of aluminum by calculation on the basis of the amount of aluminum added. The dose for this product is 0.5 mL. The above lots meet this requirement.

BioPort Corporation has set limits of 0.8-1.5 mg/mL of aluminum (0.4-0.75 mg/0.5mL dose). The above lots meet this requirement.

Formaldehyde concentration was measured by colorimetry (Hantzsch method) on June 17, 1999. CBER's results are as follows:

<u>Lot #</u>	<u>Percent Formaldehyde</u>
FAV020	0.009
FAV030	0.009

CBER's requirement specifies that the free formaldehyde in the finished product be less than 0.02 percent free formaldehyde (200 ug formaldehyde per mL). The above lots meet this requirement.

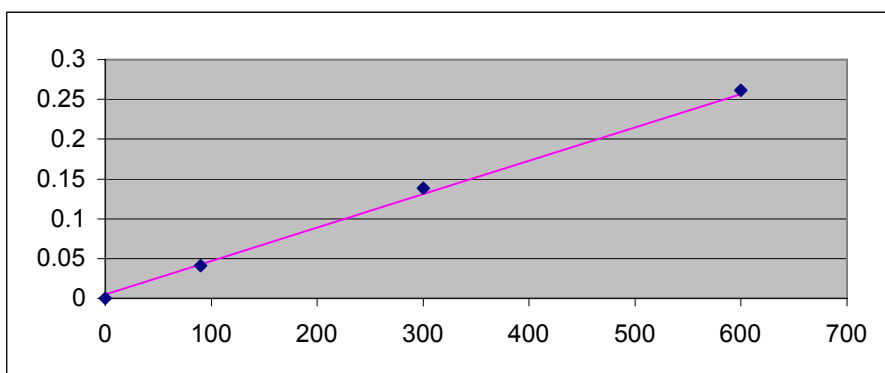
BioPort Corporation has set a limit of less than 0.02 percent formaldehyde for this product. The above lots meet this requirement.

Squalene GC

6/24/1999

File:Sq06249A

ppb Sq.	ISTD	Squalene	Squalene/ISTD
0	2329	0	0
90	2066	84	0.040658277
300	2672	370	0.138473054
600	1915	500	0.261096606
900	1720	650	0.377906977



## SUMMARY OUTPUT

<i>Regression Statistics</i>	
Multiple R	0.999346296
R Square	0.99869302
Adjusted R Square	0.99825736
Standard Error	0.006532251
Observations	5

## ANOVA

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	0.097816045	0.097816045	2292.367986	2.00615E-05
Residual	3	0.000128011	4.26703E-05		
Total	4	0.097944055			

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95.0%</i>
Intercept	0.004747641	0.004421048	1.073872457	0.361569842	-0.009322119	0.018817402	-0.009322119
X Variable 1	0.000420316	8.77877E-06	47.87867987	2.00615E-05	0.000392378	0.000448254	0.000392378

MDPH		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
FAV020			4488	244	0.054367201	Prep. Sample
			4632	231	0.049870466	118.1
						<u>107.4</u>
						112.7
						11.3

MDPH		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
FAV030			3780	163	0.043121693	Prep. Sample
			3386	175	0.051683402	91.3
						<u>111.7</u>
						101.5
						10.1

Wyeth		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
Diphtheria			3382	340	0.100532229	Prep. Sample
	3710		3047	299	0.098129308	227.9
						<u>222.2</u>
						225.0
						22.5

PM Connaught		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
Tetanus			6401	792	0.123730667	Prep. Sample
	7271		8315	1054	0.12675887	283.1
						<u>290.3</u>
						286.7
						28.7

MDPH		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
FAV038			2860	304	0.106293706	Prep. Sample
			2284	299	0.130910683	241.6
						<u>300.2</u>
						270.9
						27.1

MDPH		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
FAV043			3160	557	0.176265823	Prep. Sample
			3631	614	0.169099422	408.1
						<u>391.0</u>
						399.5
						40.0

MDPH		ISTD	Squalene	Squalene/ISTD	ppb Squalene	
FAV047			3187	1043	0.327267022	Prep. Sample
			4560	1728	0.378947368	767.3
						<u>890.3</u>
						828.8
						82.9

Benzethonium chloride, an antimicrobial preservative, was measured using an adaptation of the colorimetric titration procedure originally specified by Michigan Department of Public Health and currently used by BioPort Corporation for this product. CBER testing was performed on June 25, 1999. Results for the two subject lots along with results obtained from three other lots of anthrax vaccine are as follows:

<u>Lot #</u>	<u>Percent Benzethonium Chloride</u>
FAV020	0.0020
FAV030	0.0015
FAV008-2	0.0017
FAV031-1	0.0019
FAV038	0.0020

Limits for benzethonium chloride content of this product were specified by Michigan Department of Public Health as 0.0015 – 0.0030 %. The above lots meet this requirement.

Squalene was determined by gas chromatography with flame ionization detection following solvent extraction and concentration. Verification of the characteristic mass spectrometric fragmentation pattern obtained from the chromatographic peak was used as part of the validation of the analytical procedure. Three other lots of anthrax vaccine were tested for comparative purposes along with two lots of other bacterial vaccines containing alum adjuvants. CBER testing was performed on 6/23 and 6/24/99. Results are as follows:

<u>Lot #</u>	<u>ppb (parts-per-billion) Squalene</u>
FAV020	11
FAV030	10
FAV038	27
FAV043	40
FAV047	83
Wyeth Diptheria Lot 3710	22
Connaught Tetanus Lot 7271	29

Squalene content of the subject lots was determined to be in the level of low parts-per-billion and was comparable to levels determined in other lots of anthrax vaccine and in the other bacterial vaccines that were tested.